

AGGGAGAGTCTGCCCAAGTTTTGTATATTTTCTCACTGAGGCATCTATTAGTTTGGGCAGCAGACA
 CTGAGCAGAACGTAGCACGGCAATGCTTGGTAGCAATGCCTGTCCGGCCAGCACTCAGAAGACGGAGGCA
 GGAGAATCATAGCTTCCAGTCAGCCTCTTCTACAATATAGTCAGTTGGAAGTCAGCCAGCTTAGACAACA
 TGGAGAGCCTGTGCCGAAAGCCACTGGGTAAGCCGAATCTCAGTAGCAGAGAGCTGCCAGGGTGCCTA
 CTGC : AAAAAAAAAACCTCAAACAACAGAAGTAGGGAGGTGTAATAAAGTGTAGGGGGGTGGAATTTA
 AGCTGATGTGGACTTCCAAATAAAGTTACCTTTTAGATACCTATTTAAATCAATAGCATAGACCTGAAAC
 TGTCTATCAGAAAATGTGTCTATTCTGAGGAAGGAGTGCTAACGAGGTTCTGTGAGGGGGGCTCTGGCT
 TTGAGAGGGTGTACCATCACATAAGACTCCTAAAAGCACATACTTTTATAAATTACCATGAGCTTTAAC
 ATCTTCTTTGTCAATTCGCAGACTGAGCCATGGAGTCTTTGATGCTGACACCAATTCAACTGACCTACA
 CTCACGGCCTCTGTTTCAACCCCAAGACATTGCCTCCATGGTCATTCTTGGTCTCACTTGTCTATTGGGA
 CTGCTAGGCAATGGGCTGGTGTGTGGGTAGCTGGCGTAAAGATGAAGACGACCGTGAACACAGTCTGGT
 TCCTCCATCTCACCTGGCCGATTTCTCTGCTGCCTCTCCTTGCCCTTCTCCTTGGCTCACCTGATTCT
 CCAAGGACACTGGCCCTATGGCTTGTCTGTGCAAACTTATCCCATCCATCATTATTCTCAACATGTTT
 GCCAGTGTCTTCTGCTTACTGCCATTAGCCTGGACCGATGTCTGATAGTACATAAGCCAATCTGGTGCC
 AGAATCATCGAAACGTGAGAACCCTTCGCCATCTGTGGATGTGTCTGGGTGGTAGCCTTTGTGATGTG
 TGTGCCCGTATTTGTATACCGTGATCTGTTTATTATGGACAATCGCAGTATATGTAGATATAATTTTGAT
 TCCTCCAGGTCATATGATTATTGGGACTACGTGTACAACTAAGTCTACCAGAAAGCAATTCTACTGATA
 ACTCCACTGCTCAGCTAACTGGACATATGAATGACAGGTCAGCTCCTTCTCTGTACAGGCAAGGGATTA
 CTTTTGGACAGTTACCACTGCCCTCCAGTCACAGCCATTCCCTAACATCTCTGAAGACTCATTCTCTCTA
 GATTTCAGCAAACCAACAACCCATTATGGTGGAAAGCCTCCTAATGTCCTCACAGCCGCCGTACCCAGCG
 GGTTCCTGTTGAAGATCGTAAATCCAATACACTGAACGCTGACGCTTTTCTCTCTGCTCACACAGAACT
 TTTCCCTACTGCTTCTAGTGGTCATTTATACCCCTATGATTTCCAGGGGGATTATGTTGACCAATTCACG
 TATGACAATCATGTGCCGACACCGCTGATGGCAATAACCATCACAAGGCTGGTGGTGGGCTTCTGGTGC
 CGTTTTTTCATCATGGTAATTTGTTACAGCCTCATCGTCTTCAGAATGCGAAAAACCACTTCACCAAGTC
 TCGGAACAAAACCTTTCCGGGTGGCTGTGGCTGTGGTCACTGTCTTTTTTATCTGCTGGACTCCATACCAT
 CTTGTCTGGAGTCTCTGCTATTGATTACTGATCCAGAAAGTTCCTTGGGGGAAGCTGTGATGTCTGGGACC
 ACATGTCCATTGCTTTAGCATCTGCCAATAGTTGCTTCAACCCCTTCTGTATGCCCTCTTGGGGAAAGA
 CTTTAGGAAGAAAGCAAGACAGTCTATAAAGGGCATTCTGGAAGCAGCCTTCAGCGAAGAGCTCACGCAC
 TCTACCAACTGTACCCAAGACAAAGCCTCTTCAAAAAGAAACAATATGAGTACAGATGTGTGAAGATGTG
 GCCCTGGGAACCTAAGCAGAGTCTCTCAGGTGAACAGTGATGGATGACATGTGAGCAGGACACTTTAGACA
 ATTTGGCGACTCTCAGAGAAAGGTCTCTTATTGACATCAGCATCATTTGAAAACATTAAAGATGCAAAAT
 TTCAAGCCCCATCCCAGATGTGTTGACTCAGAATCTCTGGCCCATGGGACCAGTGTTTTAAACAGGCCCTC
 TTGTTTCCATCAGTGTTAAGTTTTACCTCATTTGGCTTAGTCTATTCCCATCCCTGACTACACCATGTGC
 AATGAATAACTTTTTTCATCTGTTTTTCAGTATTCTTTTTTTTTTCTTAGCATCATCTAAACTTCTAGTTTG
 CATGGAAGGCTGCTCTTATTGTTCTGAATGGAAGATATTCAATTTATTGTACAGTTTTGTGGTGGTGACAA
 GTGATTTTAAAGTGGGGAAAGAGACACAGTAAGAAAAGATCTATGAAAGCAGGGAGTGTGAGTTAGAGT
 TTGACAGAACACAGTGCCAAATGCCACCCACTAAAAGCAACCTGAGATAATTCCAGTGTTCATGTGAGCA
 AGTGAGCACAGATACATAAACTTTCTACTCCTGGAGTGTTTTAGAAAGTTGTAGCTTGGAGCTC
 (SEQ ID NO:1)

MESFDADTNSDLHSRPLFQPQDIASMVILGLTCLLGLLGNGLVLWVAGVKMKTTVNTVWFLHLTLADFLCC
 LSLPFLAHLILQGHWPYGLFLCKLIPSIILNMFASVLLTAISLDRCLIVHKPIWCQNHRNVRTAFAICGCVWV
 VAFVMCVPVFYRDLFIMDNRSICRYNFDSSRSYDYWDYVYKLSLPESNSTDNSTAQLTGHMNDRSAPSSV
 QARDYFWTVTTALQSQPFLTSPEDSFSLDSANQQPHYGGKPPNVLTAAVPSGFPVEDRKSNTLNADAFLSA
 HTELFPTASSGHLYPYDFQGDYVDQFTYDNHVPTPLMAITIRLVVGLVPFFIMVICYSLIVFRMRKTNFTKS
 RNKTRFVAVAVTVFFICWTPYHLVGVLILLITDPESSLGEAVMSWDHMSIALASANSFCNPFLYALLGKDFRK
 KARQSIKGILEAAFSEELTHSTNCTQDKASSKRNNMSTDV (SEQ ID NO:2)

FIGURE 1

underlined = deleted in the targeting construct (SEQ ID NO:5)

[] = sequence flanking Neo insert in targeting construct (SEQ ID NO:6 and SEQ ID NO:7)

AGGGAGAGTCTGCCCCAAGTTTTTGTATATTTTCTCACTGAGGCATCTATTCAGTTTGG
GCAGCAGACACTGAGCAGAACGTAGCACGGCAATGCTTGGTAGCAATGCCTGTCCGGCCA
GCACTCAGAAGACGGAGGCAGGAGAATCATAGCTTCCAGTCAGCCTCTTCTACAATATAG
TCAGTTGGAAGTCAGCCAGCTTAGACAACATGGAGAGCCTGT [GCCGAAAGCCACTGGGT
AAGCCCGAATCTCAGTAGCAGAGAGCTGCCCAGGGTGCGTACTGCAAAAAAAAAACCTC
AAACAACAGAAGTAGGGAGGTGTAAATAAAGTGTAGGGGGGTGGAATTTAAGCTGATGT
GGACTTCCAAATAAAGTTACCTTTTAGATACCTATTTAAATCAATAGCATAGACCTGAAA
CTGTCTATCAGAAAATGTGTCTATTCTGAGGAAGGAGTGCTAACGAGGTTCTGTGAGGGG
GGCCTCTGGCTTTGAGAGGGGTGTACCATCACATAAGACTCCTAAAAGCACATACTTTTAT
AAATTCACCATGAGCTTTAACATCTTCTTTGTCAATTCGCAGACTGAGCCATGGAGTCTT
TCGATGCTGACACCAATTCAACTGACCTACACTCACGGCCTCTGTTTCAACCCCAAGACA
TTG] CCTCCATGGTCATTCTTGGTCTCACTTGTCTATTGGGACTGCTAGGCAATGGGCTG
GTGCTGTGGGTAGCTGGCGTAAAGATGAAGACGACCGTGAACACAGTCTGGTTCCTCCAT
CTCACCTGGCCGATTTCTCTGCTGCCCTCTCCTTGCCCTTCTCCTTGGCTCACCTGATT
CTCCAAGGACACTGGCCCTAT [GGCTTGTTCCTGTGCAAACTTATCCCATCCATCATTAT
TCTCAACATGTTTGCCAGTGTCTTCTGCTTACTGCCATTAGCCTGGACCGATGTCTGAT
AGTACATAAGCCAATCTGGTGCCAGAATCATCGAAACGTGAGAACCGCCTTCGCCATCTG
TGGATGTGTCTGGGTGGTAGCCTTTGTGATGTGTGTGCCCGTATTGTATACCGTGATCT
GTTCAATTATGGACAATCGCAGTATATGTAGATATAATTTTGATTCCTCCAGGTCATATGA
TTATTGGGACTACGTGT] ACAAACTAAGTCTACCAGAAAGCAATCTACTGATAACTCCA
CTGCTCAGCTAACTGGACATATGAATGACAGGTCAGCTCCTTCTCTGTACAGGCAAGGG
ATTACTTTTGGACAGTTACCACTGCCCTCCAGTCACAGCCATTCTTAACATCTCCTGAAG
ACTCATTCTCTAGATTACAGCAAACCAACAACCCATTATGGTGGAAAGCCTCCTAATG
TCCTCACAGCCGCCGTACCCAGCGGGTTTCTGTTGAAGATCGTAAATCCAATACACTGA
ACGCTGACGCTTTTCTCTGCTCACACAGAACTTTTCCCTACTGCTTCTAGTGGTCATT
TATACCCCTATGATTTCAGGGGGGATTATGTTGACCAATTCAGTATGACAATCATGTGC
CGACACCGCTGATGGCAATAACCATCACAAGGCTGGTGGTGGGCTTCCTGGTGCCGTTTT
TCATCATGGTAATTTGTTACAGCCTCATCGTCTTCAGAATGCGAAAAACCACTTCACCA
AGTCTCGGAACAAAACCTTTCGGGTGGCTGTGGCTGTGGTCACTGTCTTTTTTATCTGCT
GGACTCCATACCATCTTGTGCGAGTCTGTCTATTGATTACTGATCCAGAAAGTTCCTTGG
GGGAAGCTGTGATGTCTGGGACCACATGTCCATTGCTTTAGCATCTGCCAATAGTTGCT
TCAACCCTTTCCTGTATGCCCTCTTGGGAAAAGACTTTAGGAAGAAAGCAAGACAGTCTA
TAAAGGGCATTCTGGAAGCAGCCTTCAGCGAAGAGCTCACGCACTCTACCAACTGTACCC
GGAACCTAAGCAGAGTTCTCAGGTGAACAGTGATGGATGACATGTGAGCAGGACACTTTA
GACAATTTGGCGACTCTCAGAGAAAGGTCTCTTATTGACATCAGCATCATTTGAAAACAT
TAAAGATGCAAAATTTCAAGCCCCATCCCAGATGTGTGACTCAGAATCTCTGGCCCATG
GGACCAGTGTTTTTAACAGGCCTTCTTGTTCCTCATCAGTGTAAAGTTTTACCTCATTGGC
TTAGTCTATTCCCATCCCTGACTACACCATGTGCAATGAATAACTTTTTTCATCTGTTTTT
AGTATTCTTTTTTTTCTTCTTAGCATCATCTAACTTCTAGTTTTGCATGGAAGGCTGCTCT
TATTGTTCTGAATGGAAGATATTCATTTATTGTACAGTTTTGTGGTGGTGACAAGTGATT
TTTAAGTGGGGAAGAGACACAGTAAGAAAAGATCTATGAAAGCAGGGAGTGTTGAGTTA
GAGTTTGACAGAACACAGTGCCAAATGCCACCCACTAAAAGCAACCTGAGATAATCCAG
TGTTCAATGTGAGCAAGTGAGCACAGATACACATAAACTTTTCTACTCCTGGAGTGTTT
TAGAAGTTGTAGCTTGAGCTC

FIGURE 2A

Gene Sequence Structure *

663 bp

Sequence Deleted

859 bp

Size of full-length
cDNA: 2658 bp

Targeting Vector* (genomic sequence)

Construct Number: 3036

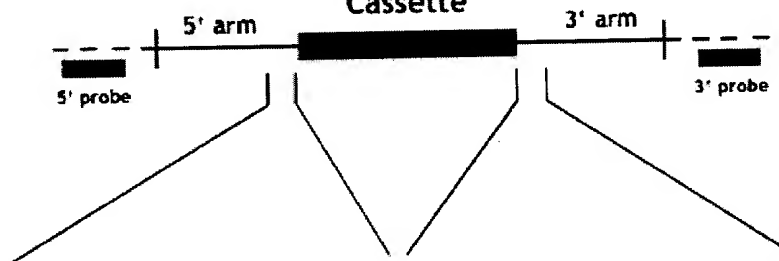
Arm Length:

5': 3.2 kb

3': 1.8 kb

LacZ-Neo

Cassette



5' >CGAGGTTCTGTGAGGGGGGCC
TCTGGCTTTGAGAGGGTGTACCAT
CACATAAGACTCCTAAAAGCACAT
ACTTTTATAAATTCACCATGAGCT
TTAACATCTTCTTTGTCATTTTCGC
AGACTGAGCCATGGAGTCTTTTCGA
TGCTGACACCAATTCAACTGACCT
ACACTCACGGCCTCTGTTTCAACC
CCAAGACATTG<3'
(SEQ ID NO:3)

5' >GGCTTGTTCTGTGCAAACCTT
ATCCCATCCATCATTATTCTCAAC
ATGTTTGCCAGTGTCTTCCTGCTT
ACTGCCATTAGCCTGGACCGATGT
CTGATAGTACATAAGCCAATCTGG
TGCCAGAATCATCGAAACGTGAGA
ACCGCCTTCGCCATCTGTGGATGT
GTCTGGGTGGTAGCCTTGTGATG
TGTGTGCCCCGT<3'
(SEQ ID NO:4)

———— Targeting Vector
----- Endogenous Locus

* Not drawn to scale

FIGURE 2B

necropsy - thymus weight/body weight

